

Claims

1. Process for the production of a conjugate from a polynucleotide and a polysaccharide comprising the steps:
  - a) provision of an aldonic acid of the polysaccharide or of a derivative thereof;
  - b) reaction of the aldonic acid with an alcohol derivative, preferably a carbonate derivative of an alcohol, to an aldonic acid ester, preferably to an activated aldonic acid ester; and
  - c) reaction of the aldonic acid ester with the polynucleotide, wherein the polynucleotide exhibits a functional amino group,  
characterised in that the reaction of the aldonic acid with the alcohol derivative in step b) takes place in a dry aprotic polar solvent.
2. Process according to claim 1, characterised in that the solvent is selected from the group comprising dimethylsulphoxide, dimethylformamide and dimethylacetamide.
3. Process according to claim 1 or 2, characterised in that the aldonic acid ester is purified and is then used in step c).
4. Process according to claim 1 or 2, characterised in that the reaction charge from step b) is used with the aldonic acid ester directly in step c).
5. Process according to one of claims 1 to 4, characterised in that step c) is carried out at a pH range of 7 to 9, preferably 7.5 to 9 and more preferably 8.0 to 8.8.

6. Process according to claim 5, characterised in that step c) is carried out at a pH of approximately 8.4.
7. Process according to one of claims 1 to 6, characterised in that the molar ratio of aldonic acid to alcohol derivative is approximately 0.9 to 1.1, preferably approximately 1.
8. Process according to one of claims 1 to 7, characterised in that the alcohol is selected from the group comprising N-hydroxy-succinimide, sulphonated N-hydroxy-succinimide, phenol derivatives and N-hydroxy-benzotriazole.
9. Process according to one of claims 1 to 8, characterised in that the polysaccharide is selected from the group comprising dextran, hydroxyethyl starch, hydroxypropyl starch and branched starch fractions.
10. Process according to claim 9, characterised in that the polysaccharide is hydroxyethyl starch.
11. Process according to claim 10, characterised in that the hydroxyethyl starch exhibits a weight-averaged mean molecular weight of approximately 3,000 to 100,000 Dalton, preferably of approximately 5,000 to 60,000.
12. Process according to one of claims 10 or 11, characterised in that the hydroxyethyl starch exhibits a number average of the mean molecular weight of approximately 2,000 to 50,000 Dalton.
13. Process according to one of claims 10 to 12, characterised in that the hydroxyethyl starch exhibits a ratio of weight-averaged molecular weight to number average of the mean molecular weight of approximately 1.05 to 1.20.
14. Process according to one of claims 10 to 13, characterised in that the hydroxyethyl starch exhibits a molar substitution of 0.1 to 0.8, preferably of 0.4 to 0.7.

15. Process according to one of claims 10 to 14, characterised in that the hydroxyethyl starch exhibits a substitution sample expressed as the C2/C6 ratio of approximately 2 to 12, preferably of approximately 3 to 10.
16. Process according to one of claims 1 to 15, characterised in that the polynucleotide is a functional nucleic acid.
17. Process according to claim 16, characterised in that the functional nucleic acid is an aptamer or a Spiegelmer.
18. Process according to one of claims 1 to 17, characterised in that the polynucleotide exhibits a molecular weight of 300 to 50,000 Da, preferably 4,000 to 25,000 Da and more preferably 7,000 to 16,000 Da.
19. Process according to one of claims 1 to 16, characterised in that the functional amino group is a primary or secondary amino group, preferably a primary amino group.
20. Process according to one of claims 1 to 19, characterised in that the functional amino group is bound to a terminal phosphate of the polynucleotide.
21. Process according to claim 20, characterised in that the functional amino group is bound to the phosphate group via a linker.
22. Process according to one of claims 1 to 21, characterised in that the functional amino group is a 5-aminoethyl group.
23. Conjugate of a polysaccharide and a polynucleotide, obtainable according to a process according to one of claims 1 to 22.